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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,519	07/25/2003	Bernhard Keppler	8182-25US (PA32424US)	2897

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AKIN GUMP STRAUSS HAUER & FELD L.L.P.
ONE COMMERCE SQUARE
2005 MARKET STREET, SUITE 2200
PHILADELPHIA, PA 19103

EXAMINER

SHIAO, REI TSANG

ART UNIT	PAPER NUMBER
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1626

DATE MAILED: 01/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/627,519

Applicant(s)

KEPPLER, BERNHARD

Examiner

Robert Shiao

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on responses filed on 11/02/2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-41 is/are pending in the application.
- 4a) Of the above claim(s) 22-32, 40 and 41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 33-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>7/25/03, 12/18/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This application claims benefit of the foreign application:
GERMANY 101 03 565.9 with a filing date 01/26/2001.
2. Amendment including cancellation of claims 1-21 and addition of claims 22-41 in the amendment filed on November 02, 2005, is acknowledged. No new matter is found. Claims 22-41 are pending in the case. Since the newly added claims 22-41 are commensurate with the scope of the invention, therefore, claims 22-41 are prosecuted in the case.

Responses to Election/Restriction

3. Applicant's election with traverse of a group of claims 33-39, in part, a product composition and its method of use, in the reply filed on November 02, 2005, is acknowledged. The traversal is on the ground(s) that examining claims 22-32 and 40-41 along with claims 33-39 would not present additional burden on the Examiner. This is not found persuasive, and the reasons are given, *infra*.

Status of the Claims

4. Claims 22-41 are pending in the application. The scope of the invention of the elected subject matter is as follows.

Claims 33-39, in part, drawn to compositions, wherein the variable B or B' of heterocycle of formula (I) or (II) represents imidazol, pyrazole, triazol or indazol thereof, and their method of use (i.e., treating tumor), classified in class 514/548 with various subclasses.

The above mentioned withdrawn compounds which are withdrawn from consideration as being for non-elected subject matter differ materially in structure and composition from the compounds of the elected invention. The withdrawn compounds/compositions contain varying heterocycle of the variable B or B' of the formula (I), (II) or (III) having azepane, thiophene, or furanyl moiety, which differ from those of the elected invention having triazole or indazol moiety, which are chemically recognized to differ in structure and function. This recognized chemical diversity of the functional groups can be seen by the various classifications of these functional groups in the U.S. classification system, i.e., class 540 subclass 450(+) (azepane), class 549 subclass 83(+) (thiophene), class 549 subclass (200+) furan, etc. Therefore, again, the compounds which are withdrawn from consideration as being for non-elected subject matter differ materially in structure and composition and have been restricted properly.

The group set forth in the claims includes both independent and distinct inventions, and patentably distinct compounds (or species) within each invention. However, this application discloses and claims a plurality of patentably distinct inventions far too numerous to list individually. Moreover, each of these inventions contains a plurality of patentably distinct compounds, also far too numerous to list individually. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner.

Claims 33-39, in part, embraced in above elected subject matter, are prosecuted in the case. Claims 33-39, in part, not embraced in above elected

subject matter, and claims 22-32 and 40-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The requirement is still deemed proper and is therefore made **FINAL**.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 37 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter "inhibiting tumor activity", which were not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, i.e., see claim 37, line 1, and page 2 of the specification.

6. Claim 37 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of use of the instant compositions by reacting compounds of formulae (I) and (II) treating colon carcinoma or ovarian carcinoma, does not reasonably provide enablement for methods of use of the instant compositions by reacting compounds of formulae (I) and (II) treating other than colon carcinoma or ovarian carcinoma, i.e., treating leukemia or multiple myeloma. The specification does not enable any person skilled in the art to which it pertains, with

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which it is most nearly connected, to use the invention commensurate in scope with these claims, see claim 37, and page 2 of the specification.

For rejections under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1988):

- 1) Nature of invention.
- 2) State of prior art.
- 3) Level of ordinary skill in the art.
- 4) Level of predictability in the art.
- 5) Amount of direction and guidance provided by the inventor.
- 6) Existence of working examples.
- 7) Breadth of claims.
- 8) Quantity of experimentation needed to make or use the invention based on the content of the Disclosure.

See below:

1) Nature of the invention

The claim is drawn to methods of use using compositions by reacting compounds of formulae (I) and (II) without limitation of named diseases.

2) State of the prior art

The reference Keppler's DE 19612291 does not indicate which compounds/compositions of instant compounds may be useful in the claimed invention. Keppler's '291 is pertaining to preparation of ruthenium(III) complexes with tumor inhibiting properties.

3) Level of ordinary skill in the art.

The level of ordinary skill in the art is high. The claim is drawn to methods of use using compositions by reacting compounds of formulae (I) and (II) without limitation of named diseases, by the instant examples disclosed in the specification.

4) Level of predictability in the art.

The claim is drawn to methods of use using compositions by reacting compounds of formulae (I) and (II) without limitation of named diseases, there would be little predictability in the scope of claimed methods or processes.

5) Amount of direction and guidance provided by the inventor.

The claim is drawn to methods of use using compositions by reacting compounds of formulae (I) and (II) without limitation of named diseases, i.e., cancer other than colon carcinoma or ovarian carcinoma (i.e., leukemia or multiple myeloma).

6) Existence of working examples.

The claim is drawn to methods of use using compositions by reacting compounds of formulae (I) and (II) without limitation of named diseases, the specification provides only limited examples of methods.

7) Breadth of claims.

The claim is extremely broad due to the vast number of possible "methods of use using compositions by reacting compounds of formulae (I) and (II) without limitation of named diseases".

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification did not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with this claim. In particular, the specification failed to enable the skilled artisan to practice the invention without undue experimentation. The skilled artisan would have a numerous methods or processes in order to obtain "methods of use using compositions by reacting compounds of formula (I) and (II) without limitation of named diseases" as claimed. Based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims, one skilled in the art could not perform the claimed compounds without undue experimentation, see *In re Armbruster* 185 USPQ 152 CCPA 1975. Incorporation of limitation of "named diseases", i.e., colon carcinoma or ovarian carcinoma, or provide written description or references for supporting named diseases, would obviate the rejection, see claims 21 and 23, and page 2 of the specification.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 33, line 1, recites limitation "a composition obtained by the process according to claim 22", is indefinite and ambiguous. It is unclear what the composition is. Is it a composition comprising a compound of formula (I), or (II), or a compound linked together by compounds of formula (I) and (II) through a non-ionic bond, or another compounds of formula (III)? Moreover, there is a duplicated limitation, i.e., n=1 or 2, in the base claim (i.e., claim 22). Clarification and correction is required.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 33-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Keller et al. US 4,843,069.

Applicants claim compositions comprising reacting compounds of formulae (I) and (II). The instant compositions have been found on pages 1-12 of the specification.

Keller et al. disclose a composition (i.e., tablet, capsules, suspension) comprising compounds, i.e., Bis[1-sodium-(1,2,4-triazolium)] pentachloro[1-sodium-(1,2,4-triazole)ruthenate(III), imidazolium diimidazoletetrachlororuthenate (III), Bis(1-methylimidazolium) (1-methylimidazole)pentachlororuthenate (III), 4-methylimidazolium tetrachlorobis(4-methylimidazole) ruthenate (III), or 1,2,4-triazolium tetrachlorobis(1,2,4-triazole)ruthenate (III), see column 6, lines 9-27, column 9, lines 8-10, column 10, lines

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55 (i.e., Ser. No. 2), column 11, lines 3-12 (i.e., Ser. NO. 11, 14-15), or column 13.

Keller et al. compositions clearly anticipate the instant compositions comprising a compound of formula (I) reacting with a compound of formula (II), wherein the variable M represent alkali metal (i.e., sodium); the variable n is 1 or 2, the variable p, q, and r independently represents 0; the variable s represent 1; the variable X or X' represent halide (i.e., chloride); the variable B or B' independently represents a monocyclic heterocycle (i.e., triazole, imidazole, triazine).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

“Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Also see M.P.E.P. 2113.

10. Claims 33-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keller et al. US 4,843,069 in view of or Keller et al. publication, European Journal of Inorganic Chemistry (1999), (9), 1551-1555.

Applicants claim compositions as agent treating cancer comprising reacting compounds of formulae (I) and (II), or a compositions comprising a mixture of

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compound of formulae (III) and (IV). The instant compositions have been found on pages 1-12 of the specification.

Determination of the scope and content of the prior art (MPEP §2141.01)

Keller et al. '069 disclose a medicament (i.e. composition) as agents treating cancer comprising a compound of formula (I),



, wherein the variable

B represents mononuclear or polynuclear unsaturated basic heterocycle radical (i.e., triazole, pyrazole, imidazole, indazol); the variable p, q, and r independently represent 0; the variable n or m independently represent 1 or 2 (i.e., 1); the variable X represents chlorine or bromine, see columns 13 and 16. A number of examples have been particularly exemplified, see column 6, lines 9-27, column 9, lines 8-10, column 10, lines 55 (i.e., Ser. No. 2), column 11, lines 3-12 (i.e., Ser. NO. 11, 14-15), or column 16, lines 9-15.

Determination of the difference between the prior art and the claims (MPEP

§2141.02)

The difference between instant claims and Keller et al. '069 is that the variable X or X' of instant compounds of formula (I) or (II) represents halide, while Keller et al. represents chlorine or bromine.

Keller et al. publication disclose two compounds, i.e., sodium salts of trans-

tetrachlorobis (indazole)ruthenate(III) trihydrate, and trans-tetrachlorobis (indazole)ruthenate(III). Keller et al. sodium salt compounds shows a 35-fold higher solubility in water relative to the indazolium salt, see page 1551, abstract, and page 1553, right column, lines 32-62.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the claims 33-39 prima facie obvious because one would be motivated to employ the compounds of Keller et al. '069 and the inherent teachings of Keller et al. to obtain instant claimed compositions, i.e., a composition obtained from reacting compounds of formulae (I) and (II) or a composition obtained from mixing compounds of formula (III) and (IV), wherein the heterocycle ring of the variable B or B' of formula (I), (II), or (III) independently represents monocyclic or multi-cyclic heterocycle (i.e., triazole, pyrazole, imidazole, indazol), and the variable n is 1 or 2, the variable p, q, r, s, X, or X' are as defined in claim 22 or 38; the variable M represents a alkali metal (i.e., sodium) are as defined in the claims.

The motivation to make the claimed compositions derives from the expectation that the instant claimed compositions derived from known Keller et al. compounds/compositions would possess similar activities (i.e., agents treating cancer) to that which is claimed in the reference.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

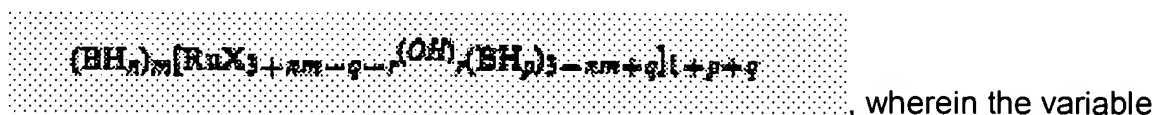
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 33-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 4 of Keppler et al. US 4,843,069 in view of or Keller et al. publication, *European Journal of Inorganic Chemistry* (1999), (9), 1551-1555. Although the conflicting claims are not identical, they are not patentably distinct from each other and reasons are as follows.

Applicants claim compositions as agent treating cancer comprising reacting compounds of formulae (I) and (II), or a compositions comprising a mixture of compound of formulae (III) and (IV). The instant compositions have been found on pages 1-12 of the specification.

Keller et al. '069 claim a medicament (i.e. compositions) as agents treating cancer comprising a compound of formula (I),



B represents mononuclear or polynuclear unsaturated basic heterocycle radical (i.e., triazole, pyrazole, imidazole, indazol); the variable p, q, and r independently represent 0; the variable n or m independently represent 1 or 2 (i.e., 1); the variable X represents chlorine or bromine, see columns 13 and 16. A number of examples have been particularly exemplified, see column 6, lines 9-27, column 9, lines 8-10, column 10, lines 55 (i.e., Ser. No. 2), column 11, lines 3-12 (i.e., Ser. NO. 11, 14-15), or column 16, lines 9-15.

The difference between instant claims and Keller et al. '069 is that the variable X or X' of instant compounds of formula (I) or (II) represents halide, while Keller et al. represents chlorine or bromine.

Keller et al. publication disclose two compounds, i.e., sodium salt of trans-tetrachlorobis (indazole)ruthenate(III) trihydrate, and trans-tetrachlorobis (indazole)ruthenate(III) Keller et al. sodium salt compounds shows a 35-fold higher solubility in water relative to the indazolium salt, see page 1551, abstract, and

page 1553, right column, lines 32-62.

One having ordinary skill in the art would find the claims 33-39 *prima facie* obvious because one would be motivated to employ the compounds of Keller et al. '069 and the inherent teachings of Keller et al. publication to obtain instant claimed compositions, i.e., a composition obtained from reacting compounds of formulae (I) and (II) or a composition obtained from mixing compounds of formulae (III) and (IV), wherein the heterocycle ring of the variable B or B' of formula (I), (II), or (III) independently represents monocyclic or multi-cyclic heterocycle (i.e., triazole, pyrazole, imidazole, indazol), and the variable n is 1 or 2, the variable p, q, r, s, X, or X' are as defined in claim 22 or 38; the variable M represents a alkali metal (i.e., sodium) are as defined in the claims.

The motivation to make the claimed compositions derives from the expectation that the instant claimed compositions derived from known Keller et al. compounds/compositions would possess similar activities (i.e., agents treating cancer) to that which is claimed in the reference.

Objection


13. Claims 33-37 are objected to not having formulae (I) and (II) of the instant compositions. Incorporation of formulae (I) and (II) and their limitation (i.e., imidazol, pyrazole, triazol or indazol of the variable B or B') of claim 22 into claims, would obviate the objection. Moreover, the phrase "and s is an integer of 1 or more" in the base claim 22 (i.e., line 15) or claim 39 is objected to having unclear limitation. Incorporation of clear limitation of variable s, i.e., 1-4, would obviate the objection.


Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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December 21, 2005


TAOFIQ SOLOLA
PRIMARY EXAMINER